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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/549,096	04/12/2000	Carl Ware	07246-030001	7342

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EXAMINER	
HUYNH, PHUONG N	
ART UNIT	PAPER NUMBER
1644	12

DATE MAILED: 03/12/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/549,096	WARE, CARL	
	Examiner	Art Unit	
	" Neon" Phuong Huynh	1644	

-- The MAILING DATE of this communication appears on the cov r sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 January 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-50* is/are pending in the application.

4a) Of the above claim(s) *1-25,33 and 37-50* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26-32 and 34-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 26-32 and 34-36 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling only for (1) A method for inhibiting a p30 polypeptide of SEQ ID NO: 6 mediated cellular response comprising a) providing a HSV gD-1 protein that inhibits binding of a cell surface expressed HVEM ligand (also known as LIGHT t66), which is a soluble homotrimeric p30 polypeptide consisting of SEQ ID NO: 6 to a cell surface expressed HVEM in vitro, which is a receptor or lymphotoxin beta receptor (LTβR), and b) contacting the cell surface expressed p30 polypeptide of SEQ ID NO: 6 or the cell surface expressed HVEM or LTβR with an amount of the composition sufficient to inhibit a p30 polypeptide of SEQ ID NO: 6-mediated cellular response wherein said composition is soluble HSV gD-1 or mouse HVEM:Fc chimeric protein or LIGHT t66; (2) The said method for inhibiting a p30 polypeptide of SEQ ID NO: 6 mediated cellular response wherein the cellular response is lymphocyte proliferation; (3) A method for inhibiting a p30 polypeptide of SEQ ID NO: 6 mediated inflammation (delayed-type hypersensitivity) in vivo comprising providing a composition that inhibits the binding of p30 polypeptide of SEQ ID NO: 6 to the HVEM receptor wherein the composition is a soluble mouse HVEM:Fc chimeric protein and (4) A method for inhibiting a p30 polypeptide of SEQ ID NO: 6 mediated collagen induced arthritis in vivo comprising providing a composition that inhibits the binding of p30 polypeptide of SEQ ID NO: 6 to the HVEM receptor wherein the composition is a soluble mouse HVEM:Fc chimeric protein (page 56); does not reasonably provide enablement for (1) A method for inhibiting *any* p30 polypeptide-mediated cellular response comprising a) providing *any* composition that inhibits binding of a cell surface expressed p30 polypeptide to a cell surface expressed HVEM or LTβR and b) contacting the cell expressing the cell surface p30 polypeptide or cell surface expressed HVEM or LTβR with an amount of *any* composition sufficient to inhibit *any* p30 polypeptide-mediated cellular response; (2) The said method wherein the cell is contacted with *any* composition *in vivo*; (3) the said method wherein *any* inhibited p30 polypeptide-mediated cellular response comprises inhibition of *any* lymphocyte cellular response; (4) The said method wherein the inhibited lymphocyte is *any* pathogenic effector cell; (5) The said method wherein the inhibited lymphocyte response modulates *any* T or B lymphoma, *any* leukemia or *any* autoimmune disease; (6) The said method wherein autoimmune disease is *any*

disease such as insulin-dependent diabetes mellitus, multiple sclerosis, systemic lupus erythematosus or myasthenia gravis; (7) The said method wherein the contacted cell expresses HVEM and the composition is any soluble p30 polypeptide; (8) The said method wherein the contacted cell expresses LTβR and the composition is any soluble p30 polypeptide, and (9) the said method wherein the contacted cell expresses any p30 polypeptide on its cell surface and the composition is any soluble HVEM polypeptide. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in **scope** with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention. The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation.

The specification discloses only three compositions wherein the composition consisting of a soluble polypeptide selected from the group consisting of HSV gD-1 protein, LIGHT t66, and HVEM:Fc chimeric protein for a method for inhibiting a p30 polypeptide of SEQ ID NO: 6 mediated cellular response comprising a) providing a HSV gD-1 protein that inhibits binding of a cell surface expressed HVEM ligand (also known as LIGHT t66), which is a soluble homotrimeric p30 polypeptide consisting of SEQ ID NO: 6 to a cell surface expressed HVEM *in vitro*, which is a receptor or lymphotoxin beta receptor (LTβR), and b) contacting the cell surface expressed p30 polypeptide of SEQ ID NO: 6 or the cell surface expressed HVEM or LTβR with an amount of the composition sufficient to inhibit a p30 polypeptide of SEQ ID NO: 6-mediated cellular response wherein said composition is soluble HSV gD-1 or mouse HVEM:Fc chimeric protein or LIGHT t66 (2) the said method for inhibiting a p30 polypeptide of SEQ ID NO: 6 mediated cellular response wherein the cellular response is lymphocyte proliferation; (3) a method for inhibiting a p30 polypeptide of SEQ ID NO: 6 mediated inflammation (delayed-type hypersensitivity) in vivo comprising providing a composition that inhibits the binding of p30 polypeptide of SEQ ID NO: 6 to the HVEM receptor wherein the composition is a soluble mouse HVEM:Fc chimeric protein; (4) a method for inhibiting a p30 polypeptide of SEQ ID NO: 6

mediated collagen induced arthritis in vivo comprising providing a composition that inhibits the binding of p30 polypeptide of SEQ ID NO: 6 to the HVEM receptor wherein the composition is a soluble mouse HVEM:Fc chimeric protein (page 56).

The specification does not teach how to make and use *any* composition for a method of inhibiting any p30 polypeptide-mediated cellular response wherein the response modulate any autoimmune immune disease such as the ones recited in claim 32. Given the indefinite number of undisclosed composition, there is insufficient guidance and working examples in the specification as filed to demonstrate that any composition could inhibit any p30 polypeptide-mediated cellular response, particularly where the "p30 polypeptide" is without structure associated with functions. Since not all p30 polypeptide expresses on the cell surface and could modulate lymphocyte cellular response, it is unpredictable which undisclosed composition could inhibit cellular response mediated by a "p30 polypeptide" having no structure and function.

With regard to autoimmune disease such as the ones recited in claim 32, other than the specific polypeptide mentioned above for inhibiting lymphocyte proliferation, delayed-type sensitivity, and collagen induced arthritis as a model for rheumatoid arthritis, the specification fails to provide sufficient in vivo working examples and guidance for treating *any* autoimmune disease such as insulin-dependent diabetes mellitus, multiple sclerosis, systemic lupus erythematosus and myasthenia gravis using any composition wherein the composition is any soluble p30 polypeptide, and any soluble HVEM polypeptide.

Van Noort et al *et al* tech that animal models of autoimmune diseases varies with respect to genetics strains, MHC haplotpes, antigen used, immunization protocols, for example, induction of autoimmune disease such as EAE with MBP does not result in the development of relapses (See page 167-170, in particular). Tian *et al* teach that in experimentally induced organ specific autoimmune disease models, the initiating antigen is defined. However, an initiating target antigen has not yet defined in human T-cell mediated autoimmune disease such as MS or IDDM (See page 190, in particular). Tian *et al* further teach that animal models of T-cell-mediated autoimmune disease rely on specific MHC genotypes and the animals often genetically predisposed to developing polarized immune response, these are likely to contribute to their disease susceptibility as well as their amenability to immunotherapy. By contrast, human MHC types are highly polymorphic, and little is known about antigen processing and presentation in this context, as well as what factors determine the nature of the immune response and possible long-term treatment (See page 193, column 1, in particular). Since treating autoimmune disease

can be species- and model-dependent, it is not clear that reliance on the collagen induced arthritis for rheumatoid arthritis using one specific HVEM:FC polypeptide accurately reflects the efficacy of the claimed method for treating other autoimmune diseases such as the ones mentioned above. Furthermore, therapeutic composition other than the specific polypeptide in the absence of in vivo data are unpredictable for the following reasons; (1) the soluble polypeptide may be inactivated before producing an effect, i.e. such as proteolytic degradation, immunological inactivation or due to an inherently short half-life of the polypeptide; (2) the polypeptide may not reach the target area because, i.e. the polypeptide may not be able to cross the mucosa or the protein may be adsorbed by fluids, cells and tissues where the protein has no effect; and (3) other functional properties, known or unknown, may make the polypeptide unsuitable for in vivo therapeutic use, i.e. such as adverse side effects prohibitive to the use of such treatment.

For these reasons, the specification as filed fails to enable one skill in the art to practice the invention as broadly as claimed without undue amount of experimentation. In re wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the decision of the court indicates that the more unpredictable the area is, the more specific enablement is necessary. As such, further research would be required. In view of the quantity of experimentation necessary, the insufficient number of working examples, the unpredictability of the art, the insufficient guidance and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

11. Claims 26-32 and 34-36 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The specification does not reasonably provide a **written description** of (1) A method for inhibiting *any* p30 polypeptide-mediated cellular response comprising a) providing any composition that inhibits binding of a cell surface expressed p30 polypeptide to a cell surface expressed HVEM or LTβR and b) contacting the cell expressing the cell surface p30 polypeptide or cell surface expressed HVEM or LTβR with an amount of any composition sufficient to inhibit any p30 polypeptide-mediated cellular response; (2) The said method wherein the cell is contacted with *any* composition *in vivo*; (3) the said method wherein any inhibited p30 polypeptide-mediated cellular response comprises inhibition of *any* lymphocyte cellular response; (4) The said method wherein the inhibited lymphocyte is any pathogenic effector cell; (5) The

said method wherein the inhibited lymphocyte response modulates any T or B lymphoma, any leukemia or any autoimmune disease; (6) The said method wherein autoimmune disease is *any* disease such as insulin-dependent diabetes mellitus, multiple sclerosis, systemic lupus erythematosus or myasthenia gravis; (7) The said method wherein the contacted cell expresses HVEM and the composition is any soluble p30 polypeptide; (8) The said method wherein the contacted cell expresses LTβR and the composition is any soluble p30 polypeptide, and (9) the said method wherein the contacted cell expresses any p30 polypeptide on its cell surface and the composition is any soluble HVEM polypeptide.

The specification discloses only three compositions wherein the composition consisting of a soluble polypeptide selected from the group consisting of HSV gD-1 protein, LIGHT t66, and HVEM:Fc chimeric protein for a method for inhibiting a p30 polypeptide of SEQ ID NO: 6 mediated cellular response comprising a) providing a HSV gD-1 protein that inhibits binding of a cell surface expressed HVEM ligand (also known as LIGHT t66), which is a soluble homotrimeric p30 polypeptide consisting of SEQ ID NO: 6 to a cell surface expressed HVEM in vitro, which is a receptor or lymphotoxin beta receptor (LTβR), and b) contacting the cell surface expressed p30 polypeptide of SEQ ID NO: 6 or the cell surface expressed HVEM or LTβR with an amount of the composition sufficient to inhibit a p30 polypeptide of SEQ ID NO: 6-mediated cellular response wherein said composition is soluble HSV gD-1 or mouse HVEM:Fc chimeric protein or LIGHT t66 (2) the said method for inhibiting a p30 polypeptide of SEQ ID NO: 6 mediated cellular response wherein the cellular response is lymphocyte proliferation; (3) a method for inhibiting a p30 polypeptide of SEQ ID NO: 6 mediated inflammation (delayed-type hypersensitivity) *in vivo* comprising providing a composition that inhibits the binding of p30 polypeptide of SEQ ID NO: 6 to the HVEM receptor wherein the composition is a soluble mouse HVEM:Fc chimeric protein; (4) a method for inhibiting a p30 polypeptide of SEQ ID NO: 6 mediated collagen induced arthritis in vivo comprising providing a composition that inhibits the binding of p30 polypeptide of SEQ ID NO: 6 to the HVEM receptor wherein the composition is a soluble mouse HVEM:Fc chimeric protein (page 56).

With the exception of the specific polypeptides mentioned above, there is insufficient written description about the structure associated with functions of *any* soluble p30 polypeptide, *any* soluble HVEM polypeptide as a composition for a method for inhibiting p30 polypeptide mediated cellular response such as inhibited lymphocyte proliferation in rheumatoid arthritis.

Given the lack of a written description of *any* additional representative species of polypeptides for a composition used in a method, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.*

Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

12. INFORMATION ON HOW TO EFFECT DRAWING CHANGES

Correction of Informalities -- 37 CFR 1.85

New corrected drawings must be filed with the changes incorporated therein. Identifying indicia, if provided, should include the title of the invention, inventor's name, and application number, or docket number (if any) if an application number has not been assigned to the application. If this information is provided, it must be placed on the front of each sheet and centered within the top margin. If corrected drawings are required in a Notice of Allowability (PTOL-37), the new drawings **MUST** be filed within the **THREE MONTH** shortened statutory period set for reply in the "Notice of Allowability." Extensions of time may NOT be obtained under the provisions of 37 CFR 1.136 for filing the corrected drawings after the mailing of a Notice of Allowability. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

Corrections other than Informalities Noted by Draftsperson on form PTO-948.

All changes to the drawings, other than informalities noted by the Draftsperson, **MUST** be made in the same manner as above except that, normally, a highlighted (preferably red ink) sketch of the changes to be incorporated into the new drawings **MUST** be approved by the examiner before the application will be allowed. No changes will be permitted to be made, other than correction of informalities, unless the examiner has approved the proposed changes.

Timing of Corrections

Applicant is required to submit acceptable corrected drawings within the time period set in the Office action. See 37 CFR 1.85(a). Failure to take corrective action within the set period will result in **ABANDONMENT** of the application.

13. No claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to "Neon" Phuong Huynh whose telephone number is (703) 308-4844. The examiner can normally be reached Monday through Friday from 9:00 am to 6:00 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

15. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-7401.

Phuong N. Huynh, Ph.D.
Patent Examiner
Technology Center 1600
March 11, 2002

Christina Chan
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